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(54) SKIN CARE PREPARATION

(57)Abstract:

PROBLEM TO BE SOLVED: To solve the problem that a ginseng and Panax ginseng are utilized as a crude medicine from old times, and formulated with the skin care preparation such as a cosmetic, but a skin care preparation being more effective or having stronger effectiveness is desired.

SOLUTION: This skin care preparation contains ginsenoside Rh2 and/or ginsenoside Rg3 formulated therewith.

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CLAIMS

[Claim(s)]
[Claim 1]Skin external preparations blending JINSENO side Rh_2 and/or JINSENO side Rg_3 which were produced by an enzyme treatment method

[Translation done.]

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DETAILED DESCRIPTION

[Detailed Description of the Invention]
[0001]
[Field of the Invention]This invention relates to those with a cell activation operation, such as drugs, quasi drugs, and cosmetics, and the skin external preparations which have a skin immunity adjustment operation especially. It is related with the safe and effective skin external preparations containing the extract of JINSENO side Rh_2 produced by the enzyme treatment method in more detail, and/or JINSENO side Rg_3.

[0002]
[Description of the Prior Art]The ginseng radix, the OTANE ginseng radix (it carries out abbreviated to a medicinal ginseng radix below), etc. are used more as a crude drug in ancient times, and are blended also with skin external preparations, such as cosmetics. (Each gazette of JP,50-95416,A, JP,55-127317,A, JP,58-113116,A, and JP,59-55809,A) It is widely used also as a hair restorer again. (Each gazette of JP,60-38314,A, JP,60-199810,A, JP,60-222409,A, and JP,60-255715,A) Use for cosmetics is added mainly paying attention to the work which activates a cell. By the latest research, a medicinal ginseng radix has an immunity adjustment operation, and it has also turned out that cancer is useful. It has become clear as one of the latest results of research that the effect also has strong JINSENO side Rh_2 and JINSENO side Rg_3 which are especially contained in a wild medicinal ginseng radix mostly in it.
[0003]
[Problem to be solved by the invention]Since skin external preparations including cosmetics may be used continuously over a long period of time and applied to an organ with much area called the skin, there is validity required for skin external preparations variously again by one of the items by which safety is thought as most important, and effects, such as aging prevention

of the skin and surface deterioration prevention, are searched for. That colored races, such as Japanese, have a white skin leads to beauty, and whitening is large as an effect for which skin external preparations are asked. Of course, there are maintaining so that the moisture from the inside of the body may not be lost, and an external physical protective function so that the function which the skin furthermore has can live also in the dry atmosphere, but the latest research is showing that the skin has played the important role also about immunity. Although the skin comprises a cornification cell of epidermis, Langerhans cell, a dendritic cell of dermis, a vascular endothelial cell, a macrophage, etc., To invasion of the antigen as a foreign matter from the outside, it contacts promptly and processes, and it moves to lymph gland, it is shown to a T cell, and it is thought that a series of future immune response reactions start. And being exposed to ultraviolet rays and stress also show that this immune function falls, there is a possibility of generating various skin disease (what does not result in a disease is included and they are the abnormalities of the skin) even if it does not result in oncogenesis, and normalization of skin immunity is an item which should be enough taken into consideration. And work of the immunity in the skin differs from other organs greatly, and even if it turns out that it is related to other immunity, the work by the skin differs again in many cases.

[0004]

[A means for invention to be solved] As a result of considering safety and the validity to the skin and inquiring wholeheartedly, the skin external preparations using JINSENO side Rh_2 and/or JINSENO side Rg_3 which are contained in vegetation, such as a ginseng radix, and which are useful components became clear [that it is the best for the purpose of this invention, or]. In this invention, by blending JINSENO side Rh_2 and/or JINSENO side Rg_3 which were produced using the enzyme treatment method, the skin immunity normalization effect was strong, and this invention person examined and developed the still more useful skin external preparations on the skins, such as the cell activation effect.

[0005]JINSENO side Rh_2 and/or JINSENO side Rg_3 can be extracted from what carried out processing treatment (for example, desiccation, cutting, parboiling, steam heating, or disintegration), using vegetable [containing JINSENO sides / the whole or some of] as it is. However, since the content is naturally high to a medicinal ginseng radix, it extracts from this in many cases. If the kind is illustrated, araliaceous Panax schinseng (Panaxginseng C.A.Meyer;Panax schinseng Nees), Panax japonicus (Panaxjaponicus.) C.A. Meyer;Panax schinsengNees var.japonicumMakino;Panax pseudo-ginseng (Will.) subsp.japonicus Hara, SANSHI thynnine gin (Panaxnotoginseng(Burkill) F.H.Chen;Panax sanchi Hoo;Panaxpseudo-ginseng Wallich var.notoginseng(Burkill) Hoo.) et Tseng or a U.S. ginseng (Panax quinquefolium L.) can be mentioned. It is also possible for JINSENO side Rh_2 and/or JINSENO

side Rg_3 to choose and culture the cell contained mostly, and to obtain from a medicinal ginseng radix in large quantities. For example, the root of an OTANE ginseng radix and a growing point is cultivated, and if a cell with many yields is chosen in it, it can obtain in large quantities. As it is in JP,H8-208688,A, it is compoundable also from a terpene. In this invention, a lot of JINSENO side Rh_2 and/or JINSENO side Rg_3 were obtained by extracting the vegetation containing many JINSENO side Rh_2 and/or JINSENO side Rg_3 after enzyme treatment. For obtaining the ginseng radix constituent of Rh_2 (1,400-1,500 mg) and Rh_3 (280-300 mg) content, it is based on the following methods. a law -- 20-30 ** of things which added 3% of wheat bran and 1% of ginseng radix powder to the liquid medium of the method, and inoculated the aspergillus of the Aspergillus group are cultivated aerobically for 60 to 80 hours. A biomass is removed by centrifugal separation after that, 50 to 80% of ethanol solution is added to culture medium, and enzyme protein is precipitated and ****(ed). Next, after remelting to 0.02M sodium acetate (pH 5.0) according to the quantity which ****(ed) the obtained enzyme protein and removing an impurity with a centrifuge method, an enzyme treatment solution is obtained as supernatant liquor. Rough saponin is made to react to an enzyme treatment solution for adequate amount **** 18 to 24 hours, and vacuum concentration of the supernatant liquor is carried out for an impurity after precipitation processing in ethanol after that. After diluting a concentrate with an acetic acid solution 20 times 50 to 70% and making it react for further 4 to 8 hours, the obtained reaction mixture is freeze-dried and a ginseng radix constituent is obtained. The extraction method from a medicinal ginseng radix (or tissue culture thing) should just use a publicly known method. The example is given to below. After degreasing using an organic solvent, for example, hexane, and petroleum ether as occasion demands, It evaporates to dryness, after add n-butanol, dissolving, after extracting using water, lower aliphatic alcohol (for example, methanol, ethanol), or water and lower aliphatic alcohol and removing a solvent, adding water to this, stirring and taking out n-butanol layer. A residue is melted in lower aliphatic alcohol and the sludge obtained by carrying out stirring pouring in ether is ****(ed). What is necessary is just to isolate JINSENO side Rh_2 and JINSENO side Rg_3 preparatively for this using chromatography. Compounding furthermore is also possible, and if an example is given, it can also obtain with a manufacturing method like JP,H3-208688,A. What is necessary is for there to be no limitation in purity, and for all and a case to also adjust the degree of refining and just to use them by cost, a use, etc.

[0006]Although JINSENO side Rh_2 and/or JINSENO side Rg_3 are blended with skin external preparations, and it changes with an extraction method, combination purposes, etc., 0.0001 to 10.0% of loadings are desirable as solid content. Although what is necessary is just to choose freely since other raw materials to blend are not limited, it stands to reason that a raw material

which is not contrary to the meaning of skin external preparations which have validity by safety of this invention is chosen. For this reason, using together with various kinds of drugs which have an effect in whitening, antioxidation and cell activation (cellular senescence prevention), moisturization, surface deterioration prevention, its improvement, etc. makes the purpose of this invention still more effective. A problem does not have choosing from arbitrary pharmaceutical forms, such as cream, a milky lotion, a lotion, a pack, a spray, and gell, by a use etc. in any way.

[0007]Although an embodiment which blended with below an example of manufacture which is an example of a actual extraction method, and an example of manufacture is indicated, naturally it is not limited to these.

[0008]After example of manufacture-1 enzyme treatment, extract 200 g for a ginseng radix heat-treated at 120 ** for 2 hours by 500 ml of ethanol, and an ethanol extract is obtained, After making the remaining residue after evaporating ethanol and removing suspend with 200 ml of water and extracting it 3 times every 200-ml ether, butanol extraction liquid which extracted 3 times at a time 200-ml butanol saturated with water in the remaining water layers, and saponin contained was obtained. 2.7 g of fractionation which contains JINSENO side Rg_3 which dries this butanol extraction liquid and carries out silica gel column chromatography using a mixed solvent of ethyl acetate / methanol / water (20:1:1) as an eluting agent, and which is made into the purpose 60% was acquired.

[0009]0.13g of JINSENO side Rh_2 was obtained by same method as example of example of manufacture-2 manufacture-1.

[0010]an embodiment is the formula shown in Table 1 -- A and B -- 80 ** -- warming -- it dissolves, and in addition, it emulsifies gradually, agitating B to A. Agitating, it cooled and cream was created by a method of stopping and neglecting churning at 35 **.

[0011]

[Table 1]

		実施例1	実施例2	実施例3	実施例4	比較例
A	スクワラン	10.0	10.0	10.0	10.0	10.0
	パルミチン酸セチル	3.0	3.0	3.0	3.0	3.0
	2-エチルヘキサン酸セチル	1.0	1.0	1.0	1.0	1.0
	トリ 2-エチルヘキサン酸グリセリル	5.0	5.0	5.0	5.0	5.0
	オリーブ油	2.0	2.0	2.0	2.0	2.0
	ベヘニルアルコール	4.0	4.0	4.0	4.0	4.0
	ステアリン酸	3.0	3.0	3.0	3.0	3.0
	メチルポリシロキサン(300cSt)	0.2	0.2	0.2	0.2	0.2
	水素添加大豆リン脂質	0.2	0.2	0.2	0.2	0.2
	モノステアリン酸 POE(15)グリセリル	0.2	0.2	0.2	0.2	0.2
	親油型モノステアリン酸グリセリル	1.0	1.0	1.0	1.0	1.0
	モノステアリン酸 POE(20)ソルビタン	0.5	0.5	0.5	0.5	0.5
	テトラオレイン酸 POE(40)ソルビトール	0.5	0.5	0.5	0.5	0.5
B	精製水	61.2	62.1	62.19	60.8	62.2
	1,3-ブチレングリコール	5.0	5.0	5.0	5.0	5.0
	パラオキシ安息香酸メチル	0.2	0.2	0.2	0.2	0.2
	グリセリン	3.0	3.0	3.0	3.0	3.0
	製造例1	1.0		0.01	1.0	
	製造例2		0.1		0.4	

[0012]The following experiments were conducted in order to check an effect. Examination 1 A skin immune-function recovery examination 8-week old C3 H/HeN male mouse was divided into four groups, and continuous irradiation of the ultraviolet rays of 10 mJ/cm^2 / day was carried out to an abdomen which a mouse of the 1st group - the 3rd group shaved for four days. The 2% liquid (a solvent is 50% ethanol) of the examples 1-2 of its the manufacture of its was applied to an irradiated part of a mouse of the 1st group - the 2nd group 50 microl./day immediately after an exposure on the 4th on the 3rd on the 2nd on the 1st. Nothing was applied to an irradiated part of a mouse of the 3rd group. The 4th group was not irradiated with ultraviolet rays. one day after the end of an exposure, contact allergy

sensitization by a dinitrofluorobenzene (DNFB) was performed in an irradiated part (in a mouse of the 4th group -- an irradiated part of a mouse of the 1st group - the 3rd group -- abbreviated -- the same abdomen). Furthermore, it caused in both ears pinna five days after sensitization, a value (value which lengthened thickness of an ear pinna before inducement from thickness of an ear pinna one day after inducement) of swelling of both ears pinna was measured further the one day afterward, and a recovery factor (%) of a contact allergy reaction was computed with a following formula.

[0013]Recovery-factor =(a-b) x100/(c-b)

[0014]However, a expresses the value of the ear-pinna swelling of the 1st group - the 2nd group, b expresses the value of the ear-pinna swelling of the 3rd group, and c expresses the value of the ear-pinna swelling of the 4th group. A result is shown in Table 2.

[0015]

[Table 2]

試験群（製造例）	回復率（%）
第1群（製造例1）	88．7
第2群（製造例2）	90．5

[0016]Examination 2 40 46-year-old female volunteers were divided into four groups from 21 years old of usefulness evaluation tests in people at random. I carried out the embodiment in the right face side, and got the left face side to carry out ter-die right-and-left tales-doses use of the comparative example. (Regulation in particular of quantity was not carried out) three months after -- the state of skin -- the following -- having evaluated .

On the standard below subjective evaluation, it caught and carried out about the whiteness of skin, the surface deterioration improvement effect, the beam of skin, the wrinkle improvement effect, and the paste of makeup. A result is shown in Table 3. (In addition, there was no person who appealed against the abnormalities of the skin during the test period.) The number in front expresses average value.

-3 which got worse dramatically as compared with -2 use before which got worse as compared with -1 use before which got worse as compared with 1 use [which was boiled a little and has been improved as compared with 2 use before improved as compared with 3 use before dramatically improved as compared with use before], and change-less 0 use before [0017]

[Table 3]

	実施例				比較例			
	肌荒れ改善効果	肌のはり	シワ改善効果	化粧のり	肌荒れ改善効果	肌のはり	シワ改善効果	化粧のり
第1群（実施例1）	2.6	2.5	2.3	2.4	0.2	0.1	0.2	0.3
第2群（実施例2）	2.3	2.4	2.4	1.9	0.3	0.3	0.2	0.2
第3群（実施例3）	2.1	2.1	2.0	2.0	0.3	0.3	0.2	0.1
第4群（実施例4）	2.7	2.8	2.7	2.7	0.1	−0.1	0.1	0.1

[0018]Examination 3 The safety test below a safety test was done.
3-1 It applied to the skin of the white male rabbit (three groups) which depilated primary-skin-irritation-test regions of back. The judgment performed erythema and an edema as an index by the marks method of primary-stimulus nature in after-application 24 and 48 or 72 hours. The sample used the 0.5% each solution of the examples 2 and 3 of manufacture. In all the animals, the result did not accept erythema and an edema, but was judged to be negativity.
[0019]3-2 The animal was applied to the skin of the Hartley system guinea pig (feminity, five groups) which depilated the skin accumulation stimulativeness examination regio lateralis in 0.5ml /once per and 5 times per week day. Spreading was performed for two weeks and the depilation was performed on the last spreading day of each week. The judgment performed erythema and an edema as an index by the marks method of primary-stimulus nature on the day following each spreading Japan and last spreading Japan. The sample used the 0.5% each solution of the examples 2 and 3 of manufacture. In all the animals, the result did not accept erythema and an edema at all over two weeks, but was judged to be negativity.
[0020]3-3 The regions of back of ten female guinea pigs of a with a Hartley system guinea pig (feminity, five groups) weights [330-400g] which depilated sensitization examination regions of back Hartley system were shaved, 0.5% solution 20mul of the example of manufacture was applied, and the adjuvant patch test was done. a result -- the examples 2 and 3 of manufacture -- in all the animals, neither accepted erythema and an edema but was judged to be negativity.

[0021]3-4 In accordance with the 0.5% solution 20mul conventional method of the example of manufacture, the patch test was done on 30 46-year-old female volunteers from 23 years old of Homo sapiens patch tests. (Pasting time 24 hours) a result -- the examples 2 and 3 of manufacture -- all and any [30 persons] stimulativeness in a pasting part were not accepted, either, but the stimulativeness over the human skin was judged to be negativity.

[0022]3-5 The amount internal use of 200 mg/kg of the example of manufacture was carried out at the ddy system mouse (maleness and feminity, one groups [five], 5-week old) made to abstain from food for acute toxicity test 4 hours, and progression to a toxic symptom, a grade, etc. were observed temporally. as a result, the examples 2 and 3 of manufacture -- all accepted abnormalities at all for 14 days in no mice, and the result of dissection did not have trouble, either.

[0023]

[Effect of the Invention]Recover the function of skin immunity from the examination of this invention above, and it has a function to normalize, The surface deterioration improvement effect, the beam of skin, the wrinkle improvement effect, and the paste of makeup have improved, and the skin external preparations using JINSENO side Rh_2 and/or JINSENO side Rg_3 were actually understood that validity is high as skin external preparations. It cannot be overemphasized that safety is also satisfactory at all also from the result of being made edible more in ancient times, and having done various kinds of examinations.

[Translation done.]